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Spurious Automated White Cell Count With Coulter STKS in the Myelodysplastic Syndromes Suggests the Presence of a Red Cell Membrane Defect

To the Editor: Accurate automated white cell counting requires complete red cell lysis in the white cell channel(s). Commercial lysing solutions exploit different methods of lysis. For example, the Coulter STKS utilizes a hypotonic solution and the Technicon H-1 uses a detergent, while the Cell-Dyn 3500 uses both methods, each in a separate channel [1]. Hypotonic lysis of red cells with increased osmotic resistance, e.g., neonatal red cells, may be incomplete [1,2]. We, among others [2], have encountered difficulty with automated white cell counting of neonatal blood using the Coulter STKS due to incomplete lysis of red cells. In addition to neonatal blood, problems with incomplete lysis of red cells have been seen in post-splenectomy states, megaloblastic anemia, hemoglobinopathies, and liver disease [1,3]. We would like to extend this list to include the myelodysplastic syndromes (MDS).

We have experienced difficulty with the absolute and/or differential automated white cell count in two patients with MDS.

Case 1

The first case was a 66-year-old man with refractory anemia and the following complete blood count parameters: red blood cells 2.13 million/μl, hemoglobin 7.6 g/dl, hematocrit 22.1%, mean corpuscular volume 103.9 fl, mean corpuscular hemoglobin (MCH) 35.6 pg, MCH concentration 34.2%, red cell distribution with index (RDW) 18.2, and platelet count $7 \times 10^3/\mu l$. Using the Coulter STKS, the white blood cell (WBC) count was $4.6 \times 10^3/\mu l$ with an automated differential of 30.4% neutrophils, 65.7% lymphocytes, 3.5% monocytes, 0.1% eosinophils, and 0.3% basophils. The differential count was flagged by the instrument, and the scattergram showed the presence of prominent debris in the low-volume portion of the lymphocyte area. The specimen was repeated on the Technicon H-1, which gave a total WBC count of $5.1 \times 10^3/\mu l$ and a differential count of 60.9% neutrophils, 30% lymphocytes, 4% monocytes, 0.1% eosinophils, 0.2% basophils, and 4.9% large unstained cells (LUC). A manual differential count closely matched that of the Technicon H-1.

Case 2

The second case was an 80-year-old woman with refractory anemia with excess blasts and the following complete blood count parameters: red blood cells 3.01 million/μl, hemoglobin 10.9 g/dl, hematocrit 31.8%, mean corpuscular volume 105.4 fl, MCH 36.4 pg, MCH concentration 34.4%, RDW 15, and platelet count $91 \times 10^3/\mu l$. With the Coulter STKS, the WBC count was $1.7 \times 10^3/\mu l$ with an automated differential of 17.8% neutrophils, 77.4% lymphocytes, 1.4% monocytes, 3% eosinophils, and 0.4% basophils. The instrument had no qualitative flags. However, the scattergram again showed contamination of the lymphocyte area by debris of much lower volume. The Technicon H-1 gave a total WBC count of $2 \times 10^3/\mu l$ with a differential count of 30.9% neutrophils, 56.9% lymphocytes, 1.6% monocytes, 6% eosinophils, 0.5% basophils, and 4.1% LUC. A manual differential count was essential similar to the Technicon H-1 count. Hemoglobin F measurement in both cases was $< 1\%$. In both cases the error associated with incomplete red cell lysis led to a spurious increase in the lymphocyte count and a decrease in the neutrophil count.

Osmotic fragility of red cells is related to the ratio of mean surface area (MSA) to mean cell volume [3]. Neonatal and post-splenectomy red cells have a higher content of membrane phospholipids and cholesterol, leading to an increased MSA and increased red cell resistance of hypotonic lysis [3]. Red cell membrane abnormalities are virtually unstudied in MDS. A small number of studies suggest abnormalities in membrane proteins such as spectrin, band 4.1 protein, and glycophorin C-band 4.1 protein interaction, leading to changes in osmotic fragility [4,5]. We suggest that abnormal automated white cell differential counts due to incomplete lysis of red cells by hypotonic reagents in elderly patients with unexplained cytopenias should raise the possibility of an underlying MDS. In addition, this phenomenon may help identify an interesting subgroup of MDS patients with possible abnormal red cell membrane for further studies.

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Cerebral and Vein Thrombosis, Transient Protein S Deficiency, and Anticardiolipin Antibodies

To the Editor: We report the case of a young woman with cerebral venous thrombosis associated with the presence of anticardiolipin antibodies and a transient protein S deficiency, suggesting a role for the antiphospholipid antibodies (aPL) in reducing the free protein S levels, thus determining hypercoagulable state with cerebral and venous thrombosis.

aPL have been found to be associated with recurrent spontaneous abortions and systemic arterial and venous thrombosis, as well as thrombosis of the cerebral vessels [1,2]. Recently, cases of deep vein thrombosis or severe diffuse thromboembolic disease associated with the transient presence of anticardiolipin antibodies (aCL) and functional protein S deficiency have been reported [3], suggesting a new, possibly autoimmune mechanism [4] for the thrombosis in the primary aPL syndrome. Low levels of free